C. REMARKS

The claims have been amended in order to place the application in better form.

Claim 6 has been amended in order to provide a better definition of the claimed invention. The fact that Claim 6 has been amended is not to be construed as an admission by Applicants or Applicants' attorneys that Claim 6, prior to the amendment thereof, was unpatentable.

Claims 6-8 stands rejected under 35 U.S.C. 102(b) as being anticipated by Diukman, et al.

Claims 6-8 stands rejected under 35 U.S.C. 102(b) as being anticipated by Barnes, et al.

These rejections are respectfully traversed.

The present invention, as defined broadly in Claim 6, is directed to a method of engrafting mesenchymal stem cells. The method comprises administering cells consisting essentially of mesenchymal stem cells to a fetus in utero.

Diukman discloses the administration of bone marrow containing hematopoietic stem cells to a fetus in utero while Barnes discloses the administration of human whole blood to rabbit and monkey fetuses in utero.

Neither Diukman nor Barnes discloses or even remotely suggests to one of ordinary skill in the art the administration of cells consisting essentially of mesenchymal stem cells to a fetus in utero. Therefore, neither Diukman nor Barnes anticipates applicants' method, nor do Diukman and Barnes, taken alone or in combination, render Applicants' method as claimed obvious to one of ordinary skill in the art. It is therefore respectfully requested that the rejections under 35 U.S.C. 102 (b) be reconsidered and withdrawn.

Claim 6-8 stand rejected under 35 U.S.C. 101, because the claimed invention is not supported by either a well asserted utility or a well established utility. This rejection is respectfully traversed.

The Examiner has taken the position that Applicants have focused on only one of the cited utilities, i.e., MSC transplantation may provide a "reservoir" of normal stem cells to replace defective cells as they become damaged in degenerative diseases with progressive cellular and organ damage, and have not provided any discussion for the use in (1) large scale tissue engineering, particularly for repair of musculoskeletal injury; (2) cellular therapy for diseases of

mesenchymal origin such as muscular dystrophy, osteoporosis, osteogenesis imperfecta, and collagen disorders; (3) bone marrow conditioning to facilitate engraftment of autologous or allogeneic hematopoietic stem cells; and (4) gene therapy, each of which are in part representative of the ability of the implanted cells to act in a tissue or organ to effect the desired treatment. The Examiner also takes the position that while the specification reduces to practice the in utero transplantation of mesenchymal stem cells, the specification fails to provide a nexus between the observed phenomena and the proposed utilities.

Firstly, the claims are directed to a method of engrafting mesenchymal stem cells. In the Final Rejection, the Examiner has admitted that Applicants have reduced to practice the in utero transplantation of MSCs, and have demonstrated that MSCs will distribute into various tissues and organs of the fetus.

In addition, in the second paragraph of Page 24 of the specification, it is noted that tail wounds were made in five 65-day gestation sheep at the time of MSC injections. One sheep was sacrificed at one week, and 4 sheep were sacrificed at 2 months. Human β-2 microglobulin DNA was detected by PCR in the tail wound at one week and in one of four tail wounds at 2 months. The cells expressing human β-2 microglobulin in the tail wound appeared in the dermis and dermal appendages and had the morphologic appearance of fibroblasts consistent with participation in the wound healing response. Also, as noted at Page 28, lines 14-16, Applicants noted that the presence of human fibroblast cells in tail wound sites suggests that the MSCs are capable of differentiation for repair of damaged tissues.

Thus Applicants have demonstrated in a working example that mesenchymal stem cells may be administered to a fetus in utero to repair damaged tissue. Therefore Applicants have demonstrated a utility for the claimed invention.

Assuming, solely for the sake of argument, that Applicants have not provided any evidence of use of the invention in (i) large scale tissue engineering, (ii) cellular therapy for diseases of mesenchymal origin; (iii) bone marrow conditioning; or (iv) gene therapy, the Examiner is reminded that not every embodiment of the invention must be operable in order for the claim to be valid. When a properly claimed invention meets at least one stated objective, utility under Section 101 is clearly shown. (Raytheon Co. v. Roper Corp., 220 U.S.P.Q.592(C.A.F.C.1983), at 598; Carl Zeiss Stiftung v. Reinshaw plc, 20 U.S.P.Q. 2d 1094 (C.A.F.C. 1991), at 1100.)

Applicants have demonstrated a utility for their claimed invention, and therefore the claimed invention is patentable under 35 U.S.C.101. It is therefore respectfully requested that the rejection under 35 U.S.C. 101 be reconsidered and withdrawn.

The claims stand rejected under 35 U.S.C.112, first paragraph, in that one skilled in the art would not know how to use the claimed invention. This rejection is respectfully traversed.

As noted hereinabove with respect to the rejection under 35 U.S.C.101, Applicants demonstrated that mesenchymal stem cells may be administered to a fetus in utero to repair damaged tissue.

Therefore, contrary to the Examiner's assertions, the specification clearly teaches a circumstance to practice the method as claimed, and Applicants have provided adequate guidance for a form of treatment practicing the method of engraftment as set forth broadly in the claims.

To the extent that the Examiner relies upon the Mackenzie and Santer-Nanan papers in support of the rejection, Applicants note that, as stated previously in Applicants' Amendment filed January 30, 2006, Mackenzie reported that mesenchymal stem cells engrafted into 28 of 29 sheep fetuses that were given such cells. Mackenzie then states in the paragraph bridging Pages 404 and 405 that the results of the experiments reported by Mackenzie warrant further testing of the capacity to differentiate along multiple lineages following systemic transplantation. Applicants assert that, when the entire Mackenzie paper is taken in context, Mackenzie has a reasonable expectation that different populations of mesenchymal stem cells can be implanted into fetuses in utero, whereby the mesenchymal stem cells would differentiate into various cell types in sufficient amounts, and then persist in the born animal for a sufficient amount of time in order to treat or counteract the effects of various diseases or disorders.

In addition, Santner-Nanan, in the first sentence of the conclusion of Page 105, states that "Stem cells might have great potential for tissue repair undertaken during the fetal and neonatal period."

Therefore, based on Applicants' disclosure, and what is reported by the Mackenzie and Santner-Nanan papers, one skilled in the art would have a reasonable expectation that one could, without undue experimentation, administer mesenchymal stem cells to a fetus, and such mesenchymal stem cells would differentiate into various cell types, thereby treating or counteracting the effects of various diseases and disorders.

Thus, not only do Applicants provide a working example of administering mesenchymal stem cells to a fetus in order to repair tissue damage, but also, the scientific literature provides a reasonable expectation that one may administer mesenchymal stem cells to a fetus in utero, whereby the mesenchymal stem cells will engraft in the fetus, and differentiate into various cell types to treat or counteract the effects of various disease and disorders. Thus for the above reasons and others, the specification provides an enabling disclosure, and it is therefore respectfully requested that the rejection under 35 U.S.C.112, first paragraph, be reconsidered and withdrawn.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,

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